

## LETTER TO THE EDITOR

## Expression of prostate specific antigen in male breast cancer

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Male breast cancer is uncommon, accounting for less than 1% of all breast cancers. Carcinoma metastatic to the male breast is also unusual, with metastatic prostatic carcinoma being among the most common primary sites from which such tumours derive. Metastatic prostatic cancer and primary breast cancer may be histologically indistinguishable without immunohistochemistry because both often infiltrate with a cribriform architecture. Distinguishing between primary and metastatic disease within the breast is important because the treatment options for each are radically different. Following a case in which metastatic prostatic disease was initially wrongly diagnosed as primary breast cancer, a small series of male breast cancers was examined for expression of prostate specific antigen (PSA) and prostatic acid phosphatase to assess the usefulness of these markers in making this distinction. Focal expression of PSA was found in one of 11 cases of male breast cancer. These results indicate that PSA should be used with caution in this context.

Carcinoma of the male breast is a rare tumour accounting for 0.4–0.45% of cancers in men.<sup>1,2</sup> Carcinoma metastatic to the breast also occurs infrequently. Histologically, the differential diagnosis of carcinoma in a male breast includes primary breast cancer and metastatic disease, with the prostate being the most common primary site. However, metastatic melanoma, renal cell carcinoma, and bronchial carcinoma have all been described.<sup>3–5</sup> Histologically, metastatic prostatic carcinoma and carcinoma of the breast may be indistinguishable, although it is important that they be differentiated because treatment and prognosis differ. Although immunohistochemical detection of prostate specific antigen (PSA) and prostatic acid phosphatase (PSAP) may be useful in confirming metastatic prostatic carcinoma, recent reports of PSA expression in female breast cancer<sup>6</sup> and reports of positivity in two fine needle aspirates<sup>7</sup> are of some concern. After a case in which the metastatic nature of a male breast lesion only became apparent after immunohistochemistry for PSA, we investigated a small series of known male breast cancers for the expression of these markers to establish their usefulness in distinguishing primary from secondary malignancy in this context. Our results advise caution in the interpretation of PSA expression in these cases.

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## CASE REPORT

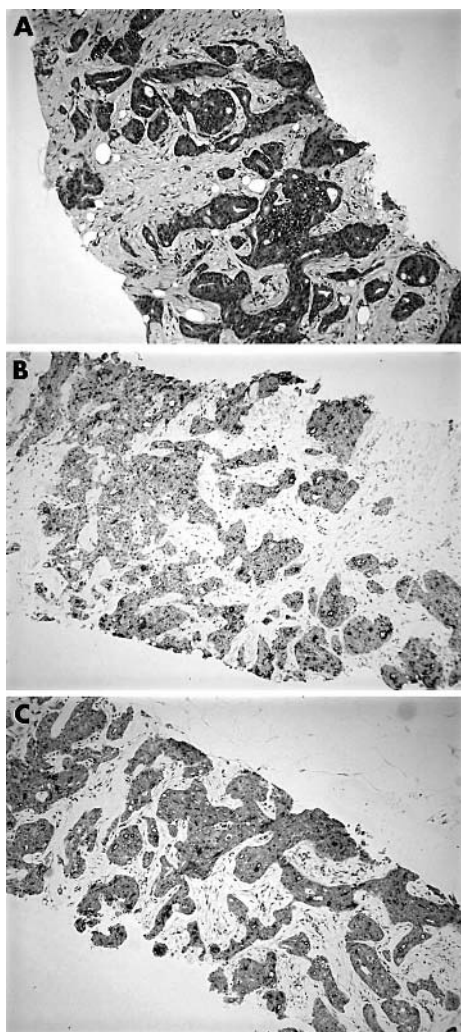
A 68 year old man was referred to the breast clinic at St James's University Hospital, Leeds, UK after presenting with

a lump in his left breast, measuring 0.5 × 1.5 cm. His hospital attendance had begun in 1992 when he presented with urgency, frequency, and intermittency of urine stream, with further investigations revealing carcinoma of the prostate, which was subsequently treated with Flutamide. In 1995, he was found to have a single solitary metastasis to the sacrum on isotope bone scanning. This responded well to Flutamide, but later the same year he developed metastatic deposits in his ribs and his serum PSA values increased. Three monthly injections of luteinising hormone releasing hormone agonist were begun. In 1997, he received Zoladex and strontium for bone pain. The breast lump developed in May 1998 and was found in the upper outer quadrant of his left breast. There was no nipple discharge and no axillary or superclavicular lymphadenopathy. A mammogram revealed an irregular mass in the 12 o'clock position and ultrasound confirmed a 13 mm irregular hypoechoic nodule. An ultrasound guided trucut biopsy was performed after a non-diagnostic (C4) fine needle aspirate.

## PATHOLOGICAL FINDINGS

The biopsy revealed an invasive carcinoma with moderately pleomorphic epithelial cells infiltrating mainly as irregular cribriform islands. The reporting pathologist had no knowledge of the previous history of prostatic carcinoma. Initially, the biopsy was reported as in keeping with an invasive ductal carcinoma of no special type, core grade 2 (tubules = 2, pleomorphism = 2, mitoses = 3) (fig 1A). The history of prostatic malignancy was revealed only at the multidisciplinary breast meeting. Subsequent review of the biopsy highlighted the need for further immunohistochemical analyses to investigate the possibility of metastatic prostatic disease. Subsequently, the tumour in the biopsy was found to be strongly positive throughout for both PSA and PSAP (fig 1B, C), but negative for oestrogen and progesterone receptors. It was decided in retrospect that the histology and presentation were more in keeping with metastatic prostatic carcinoma than with primary carcinoma of the breast. Subsequent to this case, we decided to identify cases of primary male breast cancer to clarify the usefulness of immunohistochemistry for PSA and PSAP in this context. Fourteen cases of male breast cancer were identified from the records of the Northern and Yorkshire Cancer Registry Information Service (NYCRIS) over the 15 year period from 1982 to 1997. It was possible to trace slides and blocks in 11 of these and representative blocks for immunohistochemistry were chosen. Immunohistochemistry for PSA (Dako, Ely, Cambridgeshire, UK) and PSAP (Dako) was performed on formalin fixed, paraffin wax embedded material according to standard laboratory protocols (fig 2). Table 1 shows the clinical and pathological details of the 11 cases of male breast cancer. Focal, intense cytoplasmic positivity for PSA was identified in one of the 11 cases. This was noted in an area of

**Abbreviations:** PSA, prostate specific antigen; PSAP, prostatic acid phosphatase

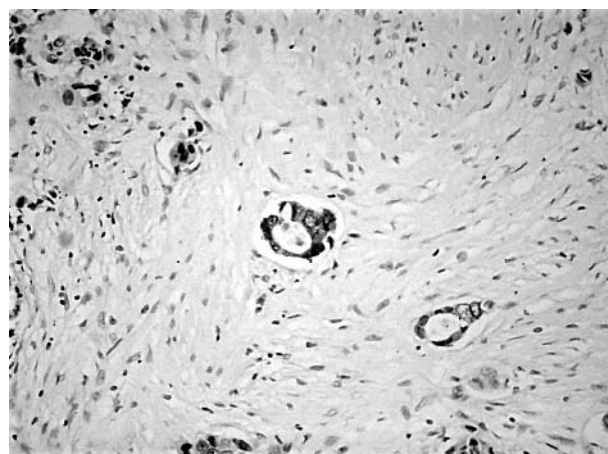


**Figure 1** (A) Core biopsy (haematoxylin and eosin) initially reported as containing invasive ductal carcinoma of no special type. (B) Tumour in the core biopsy showed strong expression of prostate specific antigen throughout. (C) Tumour in the core biopsy showed strong expression of prostatic acid phosphatase (original magnification,  $\times 20$ ).

tubule formation in an invasive ductal carcinoma of no special type, grade 3. All cases were entirely PSAP negative.

## DISCUSSION

The treatment and prognosis of primary carcinoma of the male breast and metastatic prostatic carcinoma are vastly different. Primary male breast cancer is conventionally



**Figure 2** One of 11 primary male breast cancers showed focal positive expression of prostate specific antigen (original magnification,  $\times 40$ ).

treated by wide local excision or mastectomy with axillary node clearance, and has an overall five year survival similar to that in women, varying from 37% to 84%, depending on grade and stage.<sup>8</sup> Endocrine treatment with tamoxifen may be used in oestrogen receptor positive tumours. In contrast, metastatic prostatic carcinoma has an extremely poor prognosis and surgical intervention is inappropriate. Treatment may include an oestrogen analogue, such as diethylstilboestrol, which would be contraindicated in carcinoma of the breast.

PSA is a glycoprotein produced by the prostatic epithelium, which is expressed in approximately 90% of primary prostatic carcinomas. It is used routinely in diagnostic practice to identify tissue of prostatic origin. PSAP is a tyrosine phosphatase involved in growth regulation, and is a less sensitive and specific prostatic marker, both in primary and metastatic disease. Previous reports of prostatic adenocarcinoma metastatic to the breast have emphasised the usefulness of these markers in making the distinction with primary breast cancer.<sup>9</sup> However, recent reports of PSA expression in female breast cancers<sup>6-10</sup> advise caution. This is emphasised by our finding of focal PSA expression in one of our 11 primary male breast cancers. This frequency is similar to that reported by Miller *et al*,<sup>11</sup> but less than the 23% positivity rate reported by Kidwai *et al*.<sup>12</sup> However, in agreement with our results, Kidwai *et al* found that all of their 26 cases were entirely lacking in PSAP expression. Although core biopsy has many advantages over fine needle aspiration cytology, including the provision of tissue for detailed immunophenotyping, only a limited amount of material is available for assessment.<sup>13</sup> Thus, the potential for misinterpretation of

**Table 1** Pathological details of 11 cases of male breast cancer

Case	Age	Size	Grade	Type	PSA	PSAP
1	57	70 mm	3	NST	-	-
2	78	11 mm	2	NST	-	-
3	71	25 mm	2	NST	-	-
4	73	40 mm	3	NST	-	-
5	77	20 mm	2	NST	-	-
6	70	30 mm	2	NST	-	-
7	65	17 mm	3	NST	-	-
8	61	25 mm	NA	NST	-	-
9	72	19 mm	2	NST	-	-
10	60	23 mm	3	NST	+	-
11	17 m	17 mm	1	PAPILLARY	-	-

NA, not available; NST, no special type; PSA, prostate specific antigen; PSAP, prostatic acid phosphatase.

### Take home messages

- We report a case of prostatic carcinoma metastasising to the breast, which was diagnosed only after performing immunohistochemistry for prostate specific antigen (PSA) and prostatic acid phosphatase (PSAP), subsequent to review at multidisciplinary meeting
- However, we found that PSA can be expressed in both male and female breast cancer so that this marker is only of limited use in differentiating primary breast cancer from metastatic disease in men, especially in the context of small potentially unrepresentative core biopsies.

focal PSA expression is perhaps more important in this situation.

“Prostate specific antigen may be expressed in male, in addition to female, breast cancer”

Previous reports have emphasised the role of hormones in potentially promoting metastasis of prostatic carcinoma to the breast, in addition to the development of male breast cancer.<sup>14–15</sup> Therefore, the history of treatment with Zoladex and a luteinising hormone releasing hormone agonist in our case report are of some interest. Steroid hormones and their receptors also influence PSA production, and it is possible that previous hormonal treatment may influence immunohistochemically detected expression in male breast cancer. Previous reports of mutations in the androgen response element in both breast tumours and the breast carcinoma cell line, MCF-7, suggest that this may also be involved in aberrant expression of PSA in this context, possibly altering its regulation by steroid hormones.<sup>16</sup> In female breast cancer, PSA is said to be expressed in oestrogen receptor positive, better differentiated, and earlier stage tumours, and it may be a favourable prognostic marker.<sup>17</sup> Its role in male breast cancer is unknown.

In conclusion, we report a case of prostatic carcinoma metastasising to the breast, which was diagnosed only after performing immunohistochemistry for PSA and PSAP, subsequent to review at multidisciplinary meeting, and also report an investigation into PSA and PSAP expression in a small series of male breast cancers. Focal PSA expression in one of 11 cases is described, confirming that PSA may be expressed in male, in addition to female, breast cancer. Therefore, the limitations of this marker in differentiating primary breast cancer from metastatic disease in men must

be recognised and emphasised in the context of small potentially unrepresentative core biopsies.

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